REMARKS

This application has been reviewed in light of the Office Action dated September 30, 2009. Claims 1, 3, 6-16 and 19-24 are presented for examination, of which Claims 1 and 19 ar in independent form. Claim 1 has been amended and Claims 19-24 have been added to better define the invention. Claims 17 and 18 have been cancelled. Favorable reconsideration is requested.

Claims 1, 3, 6, 7, 13 and 17 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 3,993,072 (Zaffaroni).

Claims 1, 3, 5, 13 and 16-18 had been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 5,972,372 (Saleh et al). At page 2, the Examiner indicated that this anticipation rejection had been withdrawn. However, at page 6, the Examiner has repeated an anticipation rejection and, at page 17, the Examiner has indicated that Applicants' arguments with regard to the anticipation rejection had been considered but were not persuasive but that, in view of the amendment now made to Claim 1, the rejection was now applied under 35 U.S.C. § 103(a). In the present response, Applicants have assumed that Claims 1, 3, 6, 7, 13 and 17 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,972,372 (Saleh et al).

Claims 1, 3, 6, 9-12, 14 and 15 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 3,926,188 (Baker), in view of. U.S. Patent No. 2,962,023 (Chappaz et al.).

Claims 1, 3, 6 and 8-15 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 4,217,898 (Theeuwes), in view of Zaffaroni.

Applicants respectfully traverse these rejections, particularly in view of the amendments made herein.

Prior to discussing the merits of the rejections, Applicants believe it would be helpful to discuss the advantages of the device of this invention. As noted in the specification of the present invention, vaginal rings have been difficult to effectively use, particularly when a daily release rate of a drug on the order of milligrams per day is required, for delivering hydrophilic or relatively large molecular weight (greater than 400 Daltons) drugs. See paragraphs 9-11 of the published application. It is respectfully submitted that the device of this invention, which overcome the aforementioned problem by providing a sheath that is impermeable to the at least one drug so that the at least one drug is released from the hydrophobic elastomeric polymer of the reservoir through the surface area of the reservoir that is exposed to the vaginal environment, is not suggested by the art of record.

Zaffaroni concerns itself with a porous wall whose micropores contain a drug release rate controlling medium that is permeable to the passage of the drug at a rate that is lower than the rate of passage of the drug through the reservoir itself. Thus, the rate of passage of the drug through the pores is what is controlling the release of the drug from the device itself.

Zaffaroni teaches that drug release through this medium is controlled by controlling the relative size of the pores and the molecular radius of the drug molecule. At column 9, lines 39-54, it is taught that, when the radius of the pores is at least 10 times larger than the molecular radius of the drug molecule, there is no interaction between that wall material and the drug molecule. Further on, at column 10, lines 32-39, it is taught that pores sizes from about 10 angstroms to 100 microns (0.000001mm to 0.1 mm) can be suitably employed.

The Examiner has pointed to Examples 1, 16 and 18. Example 1 concerns a drug delivery implant device containing progesterone and having a microporous cellulose coating having pores with a diameter that permits the passage of steroids. The diffusion coefficient is $2x10^{-6}cm^2sec^{-1}$. Example 16 is directed to a T-shaped intrauterine device having a reservoir containing a progestational or estrogenic antifertility steroid. The micropores are either charged with a diffusive liquid medium prior to uterine placement or are changed *in situ* with uterine biological fluid. Example 18 is directed to a vaginal ring having a microporous wall with micropores. The micropores can be pre-filled with diffusion medium or charged *in situ* with vaginal fluid.

It is clear that the micropores of Zaffaroni, which are employed along with a permeable medium to control the rate of drug diffusion, do not suggest a device having the holes or openings of the present invention, i.e., having a diameter in the range of 0.5 to 6.5 mm and the exposed claim recited surface area in a range of 1 to $750mm^2$. Zaffaroni teaches that pore sizes from 0.000001mm to 0.1 mm can be used. There is no suggestion in Zaffaroni to employ holes or openings beyond the range taught in Zaffaroni as being suitable - 0.000001mm to 0.1 mm. Applicants respectfully submit that the dimensions of the holes or openings in the intravaginal drug delivery device of the present invention, i.e., having a diameter in the range of 0.5 to 6.5 mm, are not suggested by Zaffaroni.

Saleh describes a vaginal ring having a hollow internal channel capable of receiving a drug-containing core. Salen discloses, at page 3, lines 7-12, a sealant that may be used to separate the core from the exterior environment so as to prevent passage or diffusion of the drug from the core directly to the exterior environment. Further on, in discussing the Figure 4 preferred embodiment of the invention, the term "internal" is defined as meaning no portion of

the core is exposed to, or in contact with, the outer surface of the ring body and vaginal ring is assembled and the opening is sealed (see column 6, lines 6-12). Further on, at column 6, lines 62-66, it is taught that the sealant closes the channel after core placement and minimises diffusion of the drug through the axial ends of the core. Claim 1 requires that no portion of the drug-containing core is exposed to the exterior of the vaginal ring body. In summary, although Saleh might suggest that an unsealed core could be made, it is respectfully submitted that no such embodiment is enablingly disclosed by Saleh i.e., there is no reasonable expectation of success. In fact since the whole point of Saleh is to control nausea and vomiting resulting from initial bursts of the drug, it is clear that Saleh does in fact teach away from the presently claimed invention. In the device of this invention, there is provided a sheath that is impermeable to the at least one drug so that the at least one drug is directly released from the hydrophobic elastomeric polymer of the reservoir through the surface area of the reservoir that is exposed to the vaginal environment. Applicants respectfully submit that Saleh aims to avoid initial high drug release rates. By providing a reservoir whose surface area of the reservoir that is directly exposed to the vaginal environment is in a range of 1 to 750mm^2 teaches away from the Saleh invention that aims to avoid initial burst of drug release. Therefore, it is respectfully submitted that Saleh does not render obvious the presently claimed invention.

Baker suggests that certain drugs can be dispensed at an approximately constant rate from a laminated dispenser comprising a drug-containing core partially covered with at least one rate-controlling outer lamina, provided that there is a defined correlation between the respective permeabilities, thicknesses and exposed surface areas of the core and the outer lamina(s).

The Examiner is comparing the exposed 'core edges' of Baker with the exposed core created by the holes placed in the sheath of the intravaginal drug delivery device of the present invention, such that the core of the intravaginal drug delivery device is exposed to the vaginal environment. However, the intravaginal drug delivery device of the present invention allows any number of discrete exposed drug-containing core surfaces to be exposed, limited only by the size of the intravaginal drug delivery device and the size of the holes chosen. Furthermore, Applicants can expose the reservoir on two sides, by holes in the sheath on upper and lower surfaces, or indeed more (using the inner surface of the intravaginal drug delivery device). Since the exposed core functions then as a matrix device at each exposed point, the mathematics of drug release taught by Baker, which are essentially designed to allow a balance of release from the exposed edges of the device and the sheath such that the overall effect is near-constant release, is not relevant to the intravaginal drug delivery device of the present invention. In the present application, the release is primarily always from the exposed core, because the invention has been directed at solving the problem of delivering drugs that cannot be substantially released from a conventional ring device through conventional sheath material.

Looking specifically at the mathematics of Baker, the intention, in Baker, is to have a 'balance' such that drug release is primarily through the sheath, thus giving predominantly linear (zero order) drug release, with as little release as possible through the edges. In the intravaginal drug delivery device of the present invention, the opposite is true - Applicants have, for relatively hydrophilic and/or relatively large molecular size/volume/weight drugs, drug release exclusively through the exposed core (via the holes). Thus, in Baker at column 4, lines 16-19, it is taught that 'the subject of the invention relates to an intermediate region, where neither of these effects (release through sheath or from core-edges) predominates and drug

release is almost constant with time'. In the present invention, the intravaginal drug delivery device of the present invention is at one extreme, where drug release is exclusively from the exposed core regions. This would be comparable to release being exclusively from the edges in Baker.

The device taught by Baker and that taught by the present application have essentially opposite purposes. In *Baker*, the drug must have relatively low water solubility but, in the intravaginal drug delivery device of the present invention, the device is specifically aimed at the delivery of relatively hydrophilic and/or relatively large molecular size/volume/weight drugs from devices whose reservoirs contain the drug dispersed in a hydrophobic elastomeric polymer. In other words, the devices of the present invention are essentially hydrophobic devices.

The Baker device intends that the amount of drug directly released from the core is substantially less than the amount of drug released through the sheath and that this is how a substantially constant drug release rate is achieved (see, for example, column 3, lines 36-40). Column 4, lines 54-68 teach that the drug should have a low water solubility and that a water solubility of less than about 4%. Thus, Baker differs significantly from the presently claimed invention that provides substantial drug delivery from the core to the vaginal environment and is capable of delivering relatively hydrophilic and/or large molecular weight products in milligram doses on a daily basis. It is respectfully submitted that Baker does not suggest such a device.

Chappaz has been relied upon to show that the Chappaz Figure 2 medicator is generally cylindrical and is intended for insertion into the vaginal cavity. However, this disclosure does not overcome the deficiency of Baker. In the device of Chappaz, the entire 'core' (in the form of a semi-solid formulation) is released through holes in an applicator, whereas, in

the present application, the reservoir comprising the hydrophobic elastomeric polymer, in which the drug is dispersed, remains intact and in place. Only the drug is released into the vaginal environment. Accordingly, the present claims are not rendered obvious by Baker in view of Chappaz.

Theeuwes is directed to osmotic devices and for that osmotic device to work in an aqueous environment, the reservoir must be hydrophilic. Thus, the replacement of the hydrophilic polymer with a hydrophobic elastomeric polymer, as is required by the present invention, is not an obvious design choice. In fact, despite reciting polyvinyl chloride as a hydrophobic elastomeric polymer, the Theeuwes invention will only work in an aqueous environment with hydrophilic polymers. There is nothing in Theeuwes that would have directed a person of ordinary skill in the art to the presently claimed device so as to overcome the problems associated with the delivering relatively hydrophilic and large molecular weight drugs in milligram doses on a daily basis.

Brooke was relied upon by the Examiner for the disclosure of a slit. The claims have been amended to recite that the holes or openings are substantially circular. Thus Brookes in no longer relevant since it does not remedy the deficiencies of Theeuwes. Accordingly, the present claims are not rendered obvious by Theeuwes in view of Brooke.

In view of the foregoing amendments and remarks, Applicants respectfully request favorable reconsideration and early passage to issue of the present application.

Applicants' undersigned attorney may be reached in our New York Office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address listed below.

Respectfully submitted,

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